REMARKS

Claims 1-5, 10, 11, 14, 23, 25, 28, 31, 37, 38, 46, and 49-56 were pending in this application prior to the present amendment. Claims 10, 11, 46, 49, 50, and 52 were withdrawn from consideration leaving claims 1-5, 14, 23, 25, 28, 31, 37, 38, 51, and 53-56 subject to examination. Claims 1-3, 5, 23, 37, 38, 51, 53, 54, and 56 were rejected under 35 U.S.C. § 112, first paragraph, for lack of written description. Claims 1-5, 14, 23, 25, 28, 31, 37, and 55 were rejected under 35 U.S.C. § 102(a). Claims 1, 3, 23, 37, 38, and 53-56 were rejected under 35 U.S.C. § 102(b). Claims 1-3, 5, 14, 23, 31, 37, 38, 51, and 53-56 were rejected under 35 U.S.C. § 102(e). Each of the rejections is addressed in detail below.

Claim Amendments

Claims 5, 23, 46, and 56 have been cancelled. Claims 49, 50, and 52 have been withdrawn. Applicants note that with regard to the species election, claim 1 is a generic claim and claims 49-50 and 52 depend from and include all limitations of claim 1. Therefore, upon the allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR § 1.141.

Independent claim 1 has been amended to recite the limitation that the antibody binds to a native sequence mouse or human TACI receptor, activates NF-kB, and does not inhibit binding of native sequence human or mouse BLyS[1] to the TACI receptor. Claim 2 has been amended to recite the limitation that the antibody does not bind to a native sequence mouse or human BCMA receptor. Support for these amendments is found throughout the specification and the claims, for example, in claim 23; Examples 5-7; page 16, lines 10-26; page 19, line 37 to page 20, line 15; and page 21, lines 9 to 24.

Claim 31 has been amended to recite the limitation that the antibody comprises the three complementarity determining regions (CDRs) of the heavy chain variable domain and the three CDRs of the light chain variable domain of the 7B6.15.11 antibody produced by the hybridoma deposited with ATCC as accession number PTA-5000. Support for this amendment is found

[1] Applicants note that BLyS is also referred to as TALL-1, BAFF, or THANK. See page 1, line 23 of the specification.

throughout the specification and the claims, for example, at page 28, line 33 to page 29, line 12.

Applicants reserve the right to pursue all canceled subject matter in this or a related, future application. No new matter has been added by the present amendments.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-3, 23, 37, 38, 51, 53, 54, and 56

Claims 1-3, 23, 37, 38, 51, 53, 54, and 56 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement based on the assertion that the terms "TACI receptor," "BCMA receptor," and "BLyS" are not described in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants submit that the rejection, as applied to the current claims, should be withdrawn.

According to the Examiner, the term TACI, as defined in the specification, includes a "vast collection of unknown mutants and variants of murine or human TACI....[and] TACI derived from any mammalian species." Similarly, the term "BCMA receptor" and "BLyS" would, according to the Examiner, present the same issues, namely, that there are "specific known sequences in mouse and human, wherein the terms encompass unknown variants/mutants/species and wherein the identity of the unknown variants/mutants/species is unpredictable."

While not agreeing with the Examiner, Applicants have amended the claims to recite " a native sequence mouse or human" TACI (claim 1), BLyS (claim 1) and BCMA receptor (claim 2). As acknowledged by the Examiner, the native sequence mouse and human version of each polypeptide were known in the art and were referenced in the specification as filed, for example, in Figures 1A, 1B, 2, 3, 5A, 5B, and at page 5, line 34 to page 6, line 21.

Applicants submit that the rejection of claims 1-3, 23, 37, 38, 51, 53, 54, and 56 for lack of written description may be withdrawn.

Claim 5

Claim 5 stands rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement because, according to the Examiner, while the claim recites

an antibody that binds the same epitope as the antibody recited in the claim, the actual epitope is not identified in the specification. While not agreeing with the Examiner, Applicants have cancelled claim 5 rendering the rejection moot.

Rejection under 35 U.S.C. § 102(a)

Claims 1-5, 14, 23, 25, 28, 31, 37, and 55 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Seshasayee et al. (*Immunity* 18:279-288 (2003); "Seshasayee"). Applicants assert that, for the reasons provided below, Seshasayee is not prior art to the pending claims.

As an initial matter, Applicants note that, by way of the present amendment to the inventorship and the concurrently filed Request to Correct Inventorship under 37 C.F.R. § 1.48(a), Dr. Dhaya Seshasayee is to be added as a co-inventor of the present application and Drs. Kyung Jin Kim and Minhong Yan are to be removed.

Turning to the reference, Seshasayee has a publication date of February 2003, which is less than one year prior to the effective filing date of the application (July 25, 2003) and would therefore be considered prior art only under § 102(a). As set forth in M.P.E.P. § 2132.01, a rejection under 35 U.S.C. § 102(a) over an inventor's own publication whose authorship differs from the inventive entity may be overcome by submission of a declaration by the Applicant establishing that the article is describing Applicant's own work. Here, Applicants direct the Examiner's attention to the accompanying Declaration of Dr. Dhaya Seshasayee, Declaration of Dr. Iqbal Grewal, and Declaration of Dr. Anan Chuntharapai. In each Declaration, the named inventor attests to the fact that any description of the presently claimed invention in Seshasayee was the inventive contribution of Drs. Seshasayee, Grewal, and Chuntharapai alone, notwithstanding the inclusion of the other named authors. In view of this Declaration, Seshasayee does not constitute prior art under § 102(a). *In re Katz* 215 U.S.P.Q. 14 (C.C.P.A. 1982). This basis for the rejection may be withdrawn.

Rejection under 35 U.S.C. § 102(b)

Claims 1, 3, 23, 37, 38, and 53-56 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Ashkenzai et al. (PCT Application Publication No. WO 01/60397; "Ashkenazi") as evidenced by Seshasayee. According to the Examiner, "Ashkenazi et al. disclose humanized

anti-TACI agonist antibodies which activate the TACI receptor....Said antibodies inherently have the functional property of claim 1 because said activation of said receptor causes the functional activity recited in claim 1." For the reasons outlined below, Applicants traverse the rejection and submit that the rejection, as applied to the current claims, should be withdrawn.

The claims, as amended herein, feature an agonist antibody, or a hybridoma cell line that produces an agonist antibody, that binds to a TACI receptor, inhibits B cell proliferation, activates NF-kB, and does not inhibit BLyS binding to TACI. Representative claim 1 is reproduced below:

> Claim 1. An agonist antibody that specifically binds to a native sequence mouse or human TACI receptor, wherein said agonist antibody inhibits B cell proliferation and activates NF-kB, and wherein the antibody does not inhibit a native sequence mouse or human BLyS binding to said TACI receptor.

Ashkenazi does not teach, either explicitly or inherently, any anti-TACI antibody that possesses all the features recited in claim 1. Ashkenazi provides a general teaching of agonists and antagonists of TACI or BCMA and mentions, prophetically, the use of anti-TACI or anti-BCMA antibodies as agonists or antagonists. Ashkenazi does not describe any actual agonist anti-TACI antibody, let alone one that inhibits B cell proliferation, activates NF-kB, and does not inhibit BLyS binding to TACI, as presently claimed. Moreover, Ashkenazi's prophetic agonist anti-TACI antibodies would not "inherently have the functional property of claim 1," as stated by the Examiner, because Ashkenazi's description of the functional activity of TACI agonists directly contradicts Applicants' claimed functional activity for the agonist anti-TACI antibodies. At page 38, lines 14-21, cited below, Ashkenazi describes an agonist to TACI as one that *induces cell proliferation*, the very opposite of Applicants' claimed limitation.

> The term "agonist" is used in the broadest sense, and includes any molecule that partially or fully enhances, stimulates or activates one or more biological activities of TACI polypeptide, BCMA polypeptide, or both TACI and BCMA, in vitro, in situ, or in vivo. Examples of such biological activities of TACI and BCMA include activation of NF-KB, *induction* of immunoglobulin production and secretion, and *cell proliferation*, as well as those further reported in the literature. (Emphasis added)

According to Ashkenazi, an agonist anti-TACI antibody would induce cell proliferation, while Applicants' claims recite the limitation that the agonist anti-TACI antibody inhibits B cell proliferation. Therefore, Ashkenazi does not teach, either explicitly or inherently, all of the limitations of the claims as presently amended. Applicants respectfully request that the rejection of claims 1, 3, 23, 37, 38, and 53-56 for anticipation by Ashkenazi be withdrawn.

Rejection under 35 U.S.C. § 102(e)

Claims 1-3, 5, 14, 23, 31, 37, 38, 51, and 53-56 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Kindsvogel (U.S. Patent Application Publication No. 2007/0049735; "Kindsvogel") as evidenced by Seshasayee. According to the Examiner, "Kindsvogel teaches humanized and murine monoclonal agonist antibodies which bind TACI without binding BCMA....Said antibodies inherently have the functional property of claim 1 because said activation of said receptor causes the functional activity recited in claim 1." For the reasons outlined below, Applicants traverse the rejection and submit that the present amendments should be sufficient to overcome the rejection.

As described above, the present claims, as amended herein, feature an agonist antibody, or a hybridoma cell line that produces an agonist antibody, that binds to a TACI receptor, inhibits B cell proliferation, activates NF-kB, and does not inhibit BLyS binding to TACI. Applicants submit that Kindsvogel does not teach, either explicitly or inherently, any anti-TACI antibody that possess all the features recited in the present claims.

Kindsvogel describes three anti-TACI antibodies, used as controls in Examples 2 and 3. Of these, two antibodies (251.10 and 250.13) did not have the ability to induce NF-kB activity over background levels using a luciferase reporter construct that included NK-kB and AP1 recognition sites. The remaining antibody (248.24) had the ability to inhibit B cell proliferation and stimulate luciferase activity using the same luciferase reporter construct. However, Kindsvogel does not characterize the epitope for any of the anti-TACI antibodies, nor any binding characteristics of the antibodies. Specifically, there is no mention of whether or not any of the anti-TACI antibodies inhibit BLyS binding to TACI, a characteristic specified by the presently amended claims. Therefore, Kindsvogel does not explicitly teach all of the limitations of the current claims.

Turning to the issue of inherent anticipation, Applicants submit that the Examiner has not satisfied the requirements of a rejection based on inherency as set forth in MPEP 2112. MPEP 2112 (IV) provides the burden of proof on the Examiner for establishing inherency as follows:

> To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted)
>
> In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original)

As described above, Applicants' claims feature an agonist anti-TACI antibody that inhibits B cell proliferation, activates NF-kB, and *does not inhibit BLyS binding to TACI.* The Examiner reasons that the antibody of Kindsvogel "has the same functional activity as the 7B6.15.11 antibody, which suggests that it recognizes the same epitope." Applicants submit that this reasoning is not based in fact or technical reasoning and cannot be used to support the determination that the allegedly inherent characteristic necessarily flows from the teachings of Kindsvogel.

Agonist anti-TACI antibodies possessing similar functional activity do not *necessarily* bind to the same epitope. This fact is support by Applicants' specification, which describes the discovery of, among several anti-TACI antibodies, two anti-TACI antibodies each of which share functional activity but do not share identical binding ability. Example 7 of the specification describes the characterization of the 6D11 and 7B6.15.11 anti-TACI antibodies. Both antibodies bind TACI, inhibit B cell proliferation, and activate NK-kB. However, despite the shared functional activity, they do not share binding activity. As noted at page 85, lines 23-25, "[T]he 6D11 antibody blocked binding of BLyS to TACI; however 7B6 did not...." This

demonstration of two anti-TACI antibodies that bind to TACI and share the same agonistic activity, as measured by inhibition of B cell proliferation and NF-kB activation, but which differ in their ability to block ligand binding supports Applicants' assertion that an anti-TACI antibody that has agonistic activity does not *necessarily* inhibit BLyS from binding to TACI.

Referring to the requirements to establish inherency as set forth by the Federal Circuit in *In re Robertson* (169 F.3d 743, 745 (Fed. Cir. 1999)), and cited above, Applicants submit that the anti-TACI antibody taught by Kindsvogel does not inherently anticipate Applicants' claimed antibodies because Kindsvogel's antibody would not *necessarily* inhibit BLyS from binding to TACI, nor would it be so recognized by persons of ordinary skill.

In sum, Applicants submit that Kindsvogel does not teach, either explicitly or inherently, an agonist anti-TACI antibody that inhibits B cell proliferation, activates NF-kB, and does not inhibit BLyS binding to the TACI receptor, as presently claimed. Accordingly, Applicants respectfully request that the rejection of claims 1-3, 5, 14, 23, 31, 37, 38, 51, and 53-56 for anticipation by Kindsvogel be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance and such action is respectfully requested.

Enclosed are a Petition to extend the period for replying to the Office action for two months, to and including September 30, 2008, and a check in payment of the required extension fee.

Applicants note that a Form PTO 1449 was submitted with an Information Disclosure Statement filed on August 7, 2008, and hereby request that it be initialed and returned with the next Office action.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 26 September 2008

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AMENDMENTS TO THE INVENTORSHIP

In the inventorship, kindly amend the inventorship from Anan Chuntharapai, Iqbal Grewal, Kyung Jin Kim, and Minhong Yan to Anan Chuntharapai, Iqbal Grewal, and Dhaya Seshasayee.